HEIDI D. KLEPIN, MD: Today I'm going to talk about treating older women with breast cancer, and really focus on adjuvant decision-making. And this is the basic outline. So I'm going to touch on, which Dr. Levine already did, a little background on cancer and aging. So why are we having this dedicated conversation?

Outline, very broadly, an approach to decision-making for the older patient. And then touch on some data for tumor biology by age, some of the data on adjuvant chemotherapy and age, and then how we put that together with individualized decision-making for our older adult in context with estimating patient characteristics like their life expectancy and predicting how they will tolerate chemotherapy.

So just to start out, so why are we having this conversation? I've had some discussions earlier about the field of geriatric oncology, and will it be recognized? And the answer is, oncology is already taking care of older patients. We're all doing that. It's not just those of us who did a geriatrics fellowship. So 53% of all patients who are diagnosed with cancer today are 65 years of age or older. So this is all cancer types in the US.

68% of cancer deaths occur in patients in that age group. And almost 60% of people living with cancer or cancer survivors, those who have survived their initial cancer diagnosis and treatment, are in this age group. And this is what it looks like now. That's the current landscape.

And older adults will only keep getting older. So with the aging of the population, we're not only going to simply be seeing more older adults. We're going to be seeing more in the oldest age group. So this is data from the US Bureau of the Census, which just shows you that over time, as the population is growing, projected out to 2050, the biggest single growth subset are going to be those 75 years of age or older.

So it's not just that you're going to see more 67-year-olds. We're going to increasingly be taking care of more and more 80-year-olds and 85-year-olds and 90-year-olds. And they're all going to expect an individualized and personalized care plan. And they deserve that.

So the problem is that we have very little evidence to guide our management decisions. Surveys like yes, yes, yes, population aging. Nice, Heidi has a job. But the reality is we don't have a lot of data available to us to make a truly evidence-based decision and allow our patients to make the most evidence-based decisions for themselves.

So we all know, and I think this has been highlighted earlier a little bit, that older adults are consistently under-represented on clinical trials. So right now today about 30% of patients on let's say, NCI registration trials for new drugs, new chemotherapy drugs, are 65 years of age or older. So that means that 70% of patients on those trials, the majority who reflect our evidence base, are younger than that.

And yet, most patients we're treating are in this older age group. And then, obviously I dramatize the point here a little bit, but those older adults who do make it on to clinical trials, so where we do have data, are not representative necessarily of the patients we see in clinic. So they're the fittest patients. They met all the eligibility criteria, ECOG zero to one, normal creotinine clearance. Which 80-year-old has normal creotinine clearance if you actually calculate it and minimal comorbidities?

So when you're sitting with a patient in clinic, and your first step is to say, well, is there any data for older patients? And maybe there is. But then the next step is, well, can I really extrapolate that data for those really fit selected patients to the person I'm seeing here in clinic? So making an individualized decision-making is a challenge because we really have a hard time when we're talking to patients, giving them, I think, the optimal risk and benefit scenario.

So taking a step back, so when we're talking to patients and trying to make-- help them make the most informed treatment decision they can from a medical oncology perspective, and I think this is true in radiation oncology, surgical oncology, we think about this decision-making process. I break it down into three components. What are the characteristics of the tumor? And we've talked about that a lot today. And a lot of what you've heard about precision medicine, it's really focused on tumor characteristics.

And then the characteristics of the treatments-- so can we target our treatments better? Do the treatments work? What are the toxicities? And these are important components. That's what oncology is. That's what our training is all about. Is this tumor aggressive? Is it likely to take your life or cause you morbidity? Do I have a treatment that might be effective? What's the toxicity trade-off?

But the real black box, then, and the other equally important piece is, what are the characteristics of my patient? So the tumor doesn't exist external to the patient. And the treatment and its toxicity effects are going to be different based on the patient's profile. And when we're making an adjuvant treatment decision in particular, we need to be thinking about, what's the life expectancy of my patient?

So a breast cancer adjuvant decision not only needs take into context, is this an aggressive tumor? Do I have a treatment that might work? But also is this patient likely to live long enough to potentially see those benefits? So when you estimate benefits, you're typically saying, your 10-year benefit is this. And your five-year benefit is that. Well, I need to know how long you're likely to live without the breast-cancer diagnosis in the picture.

What is your life expectancy? What's your reserve capacity? So you're doing OK now. But if I stress you with combination chemotherapy, is the bottom going to fall out? Or are you going to be able to tolerate that the way my middle-aged patients do, for example?

And then, of course, what are your values? I'll present this whole really big extensive discussion about the tumor characteristics and the treatment. And I've assessed the patient. And based on all of these great things, here is what I recommend as a treatment plan. And I've forgotten to start out with, what are your values?

What is your value system? Are you more worried about today and your quality of life? I usually, and I think wrongly, frequently weave that in at the end when I'm already presenting them the final data plan. And obviously that's the wrong place to go-- the wrong way to go about it. It's all about what the patient values now. And then you use that to inform how you guide them through the decision-making.

So with that being said, so getting back to this paradigm, I'm going to walk you through a little bit of data on characteristics of tumor as it relates to aging, some data on treatment, and then we'll talk about this last piece and how we better characterize our patient and in forming this decision. So I'll start out with a little bit about the tumor. So what's different about the tumor in older patients and younger patients with respect to breast cancer? And a lot of this data you all may already know. This is some data that was published recently looking at differences in molecular subtypes by age in breast cancer using gene expression microarray datasets for almost 4000 patients.

And what they've shown on the x-axis, you see increasing age from the youngest age group to the oldest age group-- so the far bar on the right are the oldest patients-- and the percentages of each molecular subtype. And what you can see moving left to right is that the older you are, as a population, older patients are more likely to have luminal B and luminal A subtypes, and less likely to have basal-like subtype, which actually means-- and I think we all know this-- that in general across the board, older patients are more likely to have more favorable tumor biology than younger patients, as a population.

Now that doesn't mean that you won't see a very nasty triple negative or HER2-enriched tumor in an older patient. You see those. The distribution suggests that it's less prevalent. If you look at outcomes from molecular subtypes by age-- so just look at the subtype now-- there really isn't any difference in the implications of the molecular subtype with respect to your relapse-free survival and overall survival to a large extent. So the implications of each subtype don't differ by age. It's simply the distribution, the likelihood, that you would have one of these subtypes, does.

I also wanted to comment a little bit on this slide, which I think is interesting, looking at breast cancer recurrence over time by ER status. So this is just looking at ImmunoHistoChemical staining ER positive or negative, and looking at the hazard rate of relapse over time. Comparing on the left-hand side is the historical control panel. So what happened to people? How likely were they to recur with ER negative disease and ER positive disease over time, historically and then in a more recent cohort, 2004 to 2008?

And the blue line are ER negative patients. And what you can see is on the x-axis on each figure, you see time from diagnosis. And not surprisingly, and we know this, that ER negative patients tend to have a relapse spike earlier on. So you see that spike of early recurrence in the first two years. And then your risk of recurrence over time goes down.

And that's still true in the more modern era, although the risk of recurrence for both ER positive and ER negatives has been cut approximately in half, meaning generally attributed to increased use of effective therapies. So if you look at the percentages of patients who receive chemotherapy and anti-estrogen therapies, it's roughly doubled during this time frame. So the treatments are having an impact on recurrence. But you're still seeing this differing pattern between ER negative and ER positive.

And I highlighted the arrow on the slide on the figure B, panel B, just to remind us that the majority of older women are going to have ER positive disease. So when you think about their risk of recurrence over time, they have a relatively low, as a group, risk of recurrence that remains fairly flat, going out to about eight years, declines just a little bit.

So when you think about, at the time of diagnosis, how aggressive do I want to be with my treatment now, and how likely is that to impact them in the short term, being let's say five years, it's a very different scenario than somebody with ER negative disease. So again, reminding us to be cautious and really thinking about the risk profile for our patients and integrating that into the treatment plan.

So I want to talk a little bit about data on treatment. So it's looking back at that paradigm, what are the characteristics of treatments? And what's the data for older women specifically?

In the United States there, to my knowledge, has been only one elderly-specific adjuvant chemotherapy randomized trial. And that was led by Hy Muss, which was the CALGB 49907 trial. It's now a bit of an older trial. But it's still actually the best data we have for just patients 65 and older. So this study looked at only 65 and older, stages 1 through 3 breast cancer.

And patients were randomized to what was considered usual care at the time, which was combination chemotherapy with either CMF or Adriamycin Cytoxan. So Adriamycin Cytoxan, a two-drug regimen that was very-- still is used-- very commonly used then, given every three weeks, four times. It's a 12-week regimen. Most of the patients on this trial-- this was dealer's choice, so the oncologist was able to choose one of these two-- most patients received Adriamycin Cytoxan.

The experimental arm was capecitabine, which is an oral drug. This is a 5-FU pill, essentially pill chemotherapy, single agent. And the hope was in older patients, who we suspect have a higher risk of side effects, can we get by with an active drug that is only used as a single agent? So less toxicity, used at home, so not having to come in and out. So is this a kinder, gentler way of getting effective treatment into the older patient?

And the answer was, actually it was not equally effective. So this was a non-inferiority trial. And it was very clear that the patients on capecitabine, single-agent chemotherapy, were much more likely to relapse and had shorter survival. And these are the curves showing-- displaying that here. And you can see that the benefit in relapse starts pretty early on. So these curves are splitting pretty early after about a year.

So this study was-- it was disappointing to the investigators. But basically the take-home message was if you have an older patient that you think is fit enough for chemotherapy, you should be treating them with the standard combination regimen. And there has been no study yet to date following this up to say, well, what's the next best regimen for the older patient.

So there is data that says older patients can benefit from chemotherapy. I think we all obviously believe that. But we also know that older patients are more likely to experience toxicity. And this is just one of the studies that's looked at this. This is an analysis of data from three different clinical trials. These were all women who were on-- who were fit enough to get onto randomized clinical trials, run through the CALGB.

And they just looked at high-risk toxicities. They were looking at grade 4 toxicities. They were looking at things like treatment-related mortality. So not experiencing grade 2 toxicity, which is quite prevalent. And found that in multivariate analyses, older adults were more likely to have grade 4 hematologic toxicity, were more likely to discontinue therapy due to toxicity, and were more likely to die from either AML or MDS.

Now the AML/MDS risk is very low in absolute terms. But there is clearly an association with age. And the other important point-- they looked at treatment-related mortality. So you died as a complication of your adjuvant chemotherapy. And that was associated with age as well. And in those patients who were 65 years of age or older, the treatment-related mortality was 1.5%.

That doesn't sound high. Like, oh, you know, if this were an AML trial, that would be amazingly good. But this is adjuvant chemotherapy for breast cancer. And that means that 1.5 out of every 100 people you treated in the adjuvant setting for the possibility of benefit died as a complication of your treatment. That's very sobering.

I think these numbers are not-- I think these are somewhat historical in that we use a lot more growth factor support now. So I don't think you would see quite as high of a risk in modern trials. But the association there, the age risk profile, I think, is still there. So I think a lot of this leads us up to what we all try to do every day in practice, which is to choose wisely, to really try and choose those older adults where we feel like we are most likely to give them a tangible advantage by offering chemotherapy and avoid exposing patients who we don't think are likely to have a big benefit from the toxicities of treatment.

So this is data again, this is looking at using the Oncotype DX scores. You've probably seen a lot earlier today in your presentations on the recurrence scores and how Oncotype DX can predict in a little more of a refined way risk of recurrence, particularly in node-negative patients. This is data actually looking-- this is not elderly specific. But it's looking at your risk of nine-year recurrence and women with ER positive breast cancer who were treated with an aromatase inhibitor.

So these are all postmenopausal women. So a majority of these women are older, treated with what we would consider first line anti-estrogen therapy, and what their risk of recurrence is predicted, based on their Oncotype DX if they're node negative, which is the blue line, if they have one to three positive nodes, which is the yellow line, or four-plus positive nodes. And what I'm indicating here with the arrow is to say that the majority of older patients that we're seeing are going to be ER positive. Many of them are going to fall in either the node negative or the one-to-three node positive category.

And these data would suggest, and I think this is shown in many other studies as well, that your risk of recurrence predicted at nine years is still quite low, even with one to three positive nodes. So majority-- most of these patients are not going to benefit from adjuvant chemotherapy because your absolute difference there of benefit is going to be very small.

And this is secondary data analysis from the 49907 trial, again the trial looking at Adriamycin Cytoxan versus capecitabine. And when they looked at who derived the most benefit from chemotherapy, because this was a mixed population, ER positive and negative, the answer is-- not surprisingly-- it's those older women with ER negative tumors derived a significant benefit with respect to their overall survival, and those with ER positive tumors, for the most part, the curves are overlapping, which is on the left-hand panel, certainly out to four years.

So I want to touch on, how do we integrate some of this clinical data and some of the pathologic data in real time to try and provide some estimates for our patients with some of the available tools that we have? And you've heard a lot about Oncotype DX. You heard about MammaPrint earlier today. But there are clinical variables that are not being incorporated into just looking at the tumor as we discussed. So there are a couple of decision-making aids that I think are useful.

Most of you know about Adjuvant! Online, which is useful and is used routinely in clinical practice, I think, by most medical oncologists. One of the downsides for Adjuvant! Online, which includes-- which basically gives you an estimate of how likely you are to benefit from chemotherapy and anti-estrogen therapy is that it was derived from now a fairly old dataset. So Adjuvant! Online, its initial development dataset, is fairly dated with respect to the time in which patients were diagnosed and treated.

At the time of the development, dataset HER2 status was not routinely collected. Herceptin and its treatment effect is not included in your estimates. It also, when you think about older patients, really doesn't give you a good estimate for the older patient because the developing cohort didn't include anybody 70 years of age or older. So it's not-- I still use it. I find it useful to give you some very ballpark estimates. But it has a lot of limitations, both for older and younger patients.

There is another tool that I've been using somewhat as well, which I have highlighted here on this slide, which is the PREDICT tool. And this is also a web-based online tool that you can freely access in clinic. Many of you may have used it. And it was developed more recently to try and predict overall survival, doesn't look at recurrence, just overall survival, using a more representative dataset of patients with a broader spectrum of age and collected more recently, so in a more modern chemotherapy era. So it includes taking into account HER2 status and the benefits of anti-HER2 therapy.

So it has some advantages when we think about the older patient for those reasons. And the information that you would need to have to plug in online-- age, the mode of detection of screening-- so taking into account the differences with respect to those who were symptom-detected versus screen-detected-- and then tumor size, grade, number of nodes, ER status, HER2 status, Ki-67 status if you have it, and then what generation of chemotherapy you're planning to, or you're thinking about using.

And I typed in two hypothetical scenarios. So both of these women aged 75 years of age. And really, the only variable I changed-- so these are two centimeter tumors, grade 3, one positive node. If you change the ER status, which is an obvious variable here with respect to chemotherapy benefit, you can see a significant difference in the predicted benefit in absolute terms with respect to survival, just based on whether or not you're ER positive or negative. So the top panel shows you overall survival at five and 10 years, estimates with respect to receiving adjuvant chemotherapy or not for the 75-year-old woman who has an ER negative tumor.

So they estimate that there's a 6% absolute benefit in overall survival at five years with the characteristics that I've put in for this patient using a second generation chemotherapy regimen. So that translates into a number needed to treat of about 17. So considered fairly reasonable. So that's a reasonable number to think about if I treat 17 people with these characteristics, I prevented a death in five years. If you look at the same age patient, same tumor characteristics except for ER positive, the absolute benefit of receiving adjuvant chemotherapy with respect to living longer is less than 2%. So 1.9 the estimated number needed to treat over 50.

That is a very small benefit. I think most of us would say if you're talking to a patient about that potential benefit, you would not recommend chemotherapy in that setting. The Cambridge Breast Unit who uses, who helped develop this PREDICT tool and use this regularly-- their guidelines, the way that they frame their conversations with patients is that if the absolute benefit is less than 3%, they don't recommend chemotherapy, 3% to 5%-- they discuss it. Over 5%-- they recommend it.

So kind of giving you that, no, let's talk about it. And you make your decision. Or I'm going to come down on one side where I think you're going to benefit from this treatment. And I would say for the most part, I may be even a little more conservative than that. But that's roughly the types of numbers and the types of approaches that I would take with patients.

The other thing I wanted to comment on-- so one question is, chemotherapy or not. And then another important question, of course, which chemotherapy regimen. And I don't have the answer for that. I'm not going to come down-- there are a lot of different variables there as far as which situation you're in. But there is a lot of data on the changing patterns of chemotherapy both for younger and older patients in the last couple of years.

And I thought it was interesting, the study from 2014, which is represented on the figure on the right side of your slide here looks at patterns of chemotherapy. This is SEER/Medicare data from 2003 to 2007. And what you-- this is just for older patients. So they had to-- they showed the data for younger patients. This actually looks pretty similar. But in the older patients a little more dramatic. The yellow line is Adriamycin Cytoxan. So that's the standard go-to regimen of the last 10 years, let's say, and used in the 49907 trial.

And you can see that that use of Adriamycin Cytoxan has been plummeting in the older patient from 2003 to 2007. And what's taking its place primarily is use of Taxotere Cytoxan. So a regimen two drugs. So you're basically swapping out Taxotere for Adriamycin. So you're still using two drug combination regimen every three weeks. So a 12-week treatment.

And the reason for that is first of all, there is randomized control trial data that says Taxotere Cytoxan not specific to older patients seems to be better. So there is some overall survival advantage potentially to using Taxotere Cytoxan over Adriamycin Cytoxan. Of course, in the older patient, we try to avoid anthracyclines if we can because of the increased risk of cardiotoxicity.

So the bias is particularly in treating older patients, I'd rather not use anthracyclines if I can get away with it. So for your triple negative patients, particularly in the oldest age groups for ER positive very high-risk patients, for me, my go-to regimen is Taxotere Cytoxan as well. And I think that's true for a lot of geriatric oncologists around the country, and obviously, for many people in Texas, which is where this data was based out of.

And interestingly, so this has always been my bias based on the logic that we've just discussed, that this is a bit more of a tolerable regimen for our older patients. And this is data from the same analysis where they actually looked at hospitalization by chemotherapy regimen. So this is a very real and important outcome for our older patients. Were you hospitalized during adjuvant chemotherapy?

And there was-- the yellow or orange bars are those patients 65 years of age or older. And there is a statistically significant difference in hospitalization rate for those receiving Taxotere Cytoxan, which is the first column where the arrow is lower rates compared to all the other regimens particularly and not surprisingly your third generation, or when I talk to patients, those are your triple-drug regimens. So three drugs are likely to be more toxic than two. And of course the data is bearing that out.

And a hospitalization event is a really big deal for an older patient with respect to the chances that they might have functional decline, new comorbid conditions, decline in quality of life, and you might not get through your treatment. So you've sort of lost the potential benefits of starting adjuvant chemotherapy. So this isn't the whole picture, but certainly supportive data that this regimen is one that is reasonable to be using in the older patients.

So the last part of the talk that I want to spend a little bit of time on is individualizing our decision-making to the patient. So we think about the tumor. We have a patient with a triple negative tumor. That's high risk. That's likely to warrant consideration of chemotherapy in most patients. I have treatments that I think patients may benefit from. But do I think this patient is likely to benefit based on how long they would otherwise live and their other characteristics that might impede their treatment tolerance?

So this is just some data looking at estimating life expectancy. This is actuarial data from the US population for women. And on the x-axis you see age and years. And the years of life expectancy is what's plotted here. And this is broken down based on the top 25th percentile. So I think of those as the patients who are most fit, those really fit 25% of older patients you see in each category.

And then you have your 50th percentile, which I think of as the average older adult that I see, and then the lowest 25th percentile, those who have more comorbidity, functionally impaired. And you can see I've just highlighted 80 years of age. There is a huge spread. So an 80-year-old has an estimated life expectancy of anywhere between about five years for those with more functional impairment, or more comorbidity, to 13 years.

And I would say and argue-- and I say this all the time to our trainees-- that we routinely underestimate life expectancy for many of our patients. If you're sitting in front of an 85-year-old, you're not necessarily thinking, I think you have a 9.6 year life expectancy if they're really fit. You're probably thinking it's a little bit less than that.

So I actually have this data and this chart in my clinic room to remind myself of the ballpark that I'm in. And then I try to refine it from there based on the patient characteristics to say, if I think you're likely to live 10 years or longer, we should be talking about all these adjuvant chemotherapy treatments. We should at least be-- that should be on the table at least.

So this is some data that we published from a secondary analysis from the 49907 study. So this is just looking at what are some of the characteristics that impact life expectancy in our breast cancer patients. And actually the point of this analysis that we did was really to look at whether or not comorbidities impacted toxicity during treatment. And the answer to that was, no, not in this dataset. But what we found, which I think as an internist you would say was just proof of commonsense, comorbidity is associated with overall survival.

And what was interesting here is just that this is just self-reported comorbidity. Patient says, yes, I have these things. And if you have four or more, you see a significant difference in your expected life expectancy in these breast cancer patients in their survival. So just reminding us that comorbidity is one of those things that we collect every day in clinic that we factor into life expectancy estimates. But how do you take that and package that into a number for any individual patient?

There are some tools that can help with that. And I don't know if you're familiar with ePrognosis. But this is another online tool that I think is very useful in helping to give you some ballpark life expectancy estimates from the patient that you're seeing in clinic. So this is again freely available online. Just type in ePrognosis in the Google. And it'll come up, be your first hit. And what it looks at is this. I gave you some of the references here so you can look at their development of validation code words.

But basically the variables that they look at are BMI, general health-- so does the patient say their health is generally good, fair, poor-- certain conditions like lung disease, heart failure, diabetes, smoking, some functional questions. Can you walk a quarter of a mile? Do you need assistance in your ADLs or IADLs? Can you push large objects and can you walk a quarter of a mile? So getting at function to a large extent and then comorbidities.

And again, looking at two 75-year-old women. And you put the two drastic scenarios in here as example. So if you take a patient with a low BMI, who has chronic lung disease, diabetes, and used to smoke, needs some help with their daily activities, and was hospitalized once for her lung disease last year, her five year mortality risk is 69%. So there's almost a 70% chance that she's not going to survive past five years before you gave her breast cancer. And 10 year, obviously, the risk of mortality is even higher.

Same age woman with none of those risk factors, good general health, no major comorbidities, independent, going to the gym. Her five-year mortality rate is 6%. 10 year is only 19% or 20%. So very different people with the same chronologic age. And that has a major impact on your adjuvant chemotherapy decision.

And the last thing I want to talk about with the last few slides is thinking about what are those characteristics that actually help you predict chemotherapy toxicity in your older patient? So if I can say, well, I think you're likely to live without this cancer. I think you're likely to live at least 10 years. How likely is it that you will tolerate chemotherapy if I give it to you? And you'll see that some of the characteristics you might look at are the same. So functional status plays in in both settings.

I'm just going to walk you through data from one of the largest studies that looked at this. This was a national multisite study. We were a part of it here at Wake Forest that just looked at enrolling older adults who were starting a new chemotherapy regimen not specific to breast cancer. So all the data right now is fairly nonspecific and showing you some of the same themes. And geriatric assessment was performed prior to chemotherapy, which is primarily self-administered. And the primary outcome was predicting grade 3 to 5 toxicity.

And one of the main take-home points that has come out of this study and many others like it is that the majority of patients 65 and above who get chemotherapy are going to experience toxicity, so 53%. So I round that actually off to about half. So when I talk to patients I say the average risk of having a great 3 to 5 toxicity is about 50% for an older patient. It's much higher than in the younger patient population. And then what I'm trying to do is refine are you above that? Are you 80%? Or are you 30%?

So the geriatric assessment looked at physical function, comorbidity, cognition, social functioning, social support, psychological health, and nutrition, using standardized measures. And then what they did was they looked in multivariate analyses to say, well gosh, if the physical function survey is associated with toxicity, can we refine what's driving that and pull out the single question that if we ask you this question that's the one that's actually driving the prediction risk? And so they were able to do that in their statistical modeling.

And they came out with the risk factors you see here. Each of these contributed to predicting the risk of chemotherapy toxicity. So age was still in the mix. And to get at this question of what age seems to tip you over, in this particular dataset, above age 73 was an independent predictor of chemotherapy toxicity. The type of cancer, the type of chemotherapy you received, your hemoglobin, your creotinine clearance.

And then of the assessment questions, it was one or more falls-- have you fallen in the last six months-- hearing impairment, limitations in walking-- so just like in the life expectancy estimates. Do you need help with medications? And do you have decreased social activity because of your cancer or your health? So each of these contributed some weight, which actually the question about falls was the single of the geriatric assessment questions was the single strongest contributor.

And when you looked at creating a prediction score, giving each patient a score based on those risk factors, you can actually then differentiate patients who had a very low risk of chemotherapy toxicity, so 21% to 31%, from those who had an extremely high risk of chemotherapy toxicity of over 80%. And if you compare that to the KPS, or the standard oncology assessment of your performance status in this dataset, the KPS was not predictive of toxicity.

But the geriatric assessment score was. So this score has now been validated in the second dataset. And that has actually been-- is under review now. So it should be published within the year. A couple of other studies have been done very similar showing similar themes. And what they've done now because they were able to refine the scores to specific questions, they've created an online predictive tool that you can also access. I have the website on the next slide.

Basically, most of this data you have, you either have it from the medical chart or from the decisions that you're planning to make. And you have to ask only a few questions-- falls, walking a block, can you take your medications, do you need-- do you have any interference with your social activities? And that's it.

So if you do that with every assessment, you now can plug these numbers in and actually calculate a risk of chemotherapy toxicity for an individual patient sitting in front of you. And while this is not perfect, and it's not specific to breast cancer, the data that's coming out is showing that more or less, the same risk factors are popping up in all the studies that are-- more or less its physical function, its falls, its comorbidity and creotinine clearance, for example. So this is going to give you a better prediction than what you would likely have with standard oncology assessment.

So in conclusion, decision-making for older adults needs to be individualized, looking both at the tumor and the treatment and the patient characteristics. And I think we talked a little bit about precision medicine earlier today. And I think the final frontier of precision medicine is adding that piece of really incorporating detailed assessment of the old-- or the individual patient to the tumor and the treatment. Appropriately selected older women certainly tolerate and benefit from chemotherapy.

But the emphasis needs to be on really individualizing the selection and the treatment decision. And I tried to highlight some available decision tools that you can use readily in practice, online available tools that can help you both in refining your decision and in explaining your decisions to patients, and letting them make the final choice.

So that's all I have. Thank you for your attention.